



Clostridium difficile (CDI) Infections Toolkit

Activity C: ELC Prevention Collaboratives

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Draft - 12/23/09 --- Disclaimer: The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



Outline



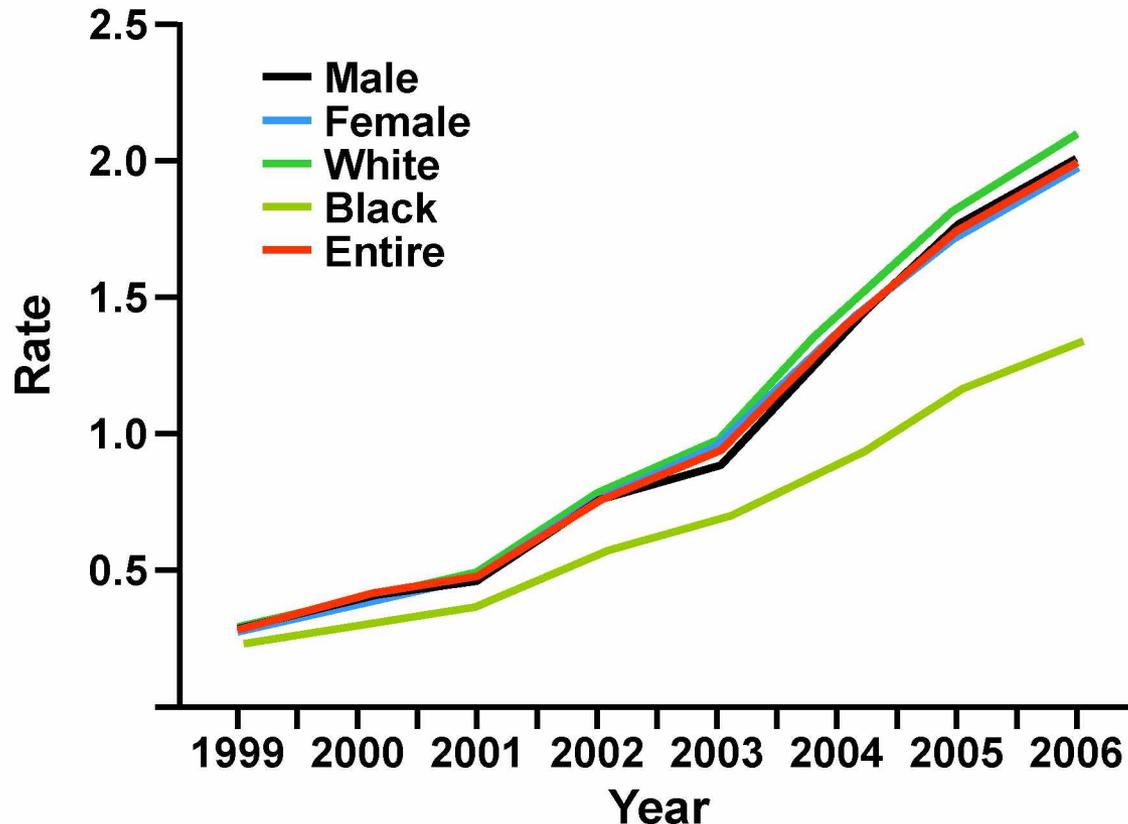
- **Background**
 - Impact
 - HHS Prevention Targets
 - Pathogenesis
 - Epidemiology
- **Prevention Strategies**
 - Core
 - Supplemental
- **Measurement**
 - Process
 - Outcome
- **Tools for Implementation/Resources/References**



Background: Impact



Age-Adjusted Death Rate* for Enterocolitis Due to *C. difficile*, 1999–2006



*Per 100,000 US standard population

Heron et al. Natl Vital Stat Rep 2009;57(14).

Available at http://www.cdc.gov/nchs/data/nvsr/nvsr57/nvsr57_14.pdf



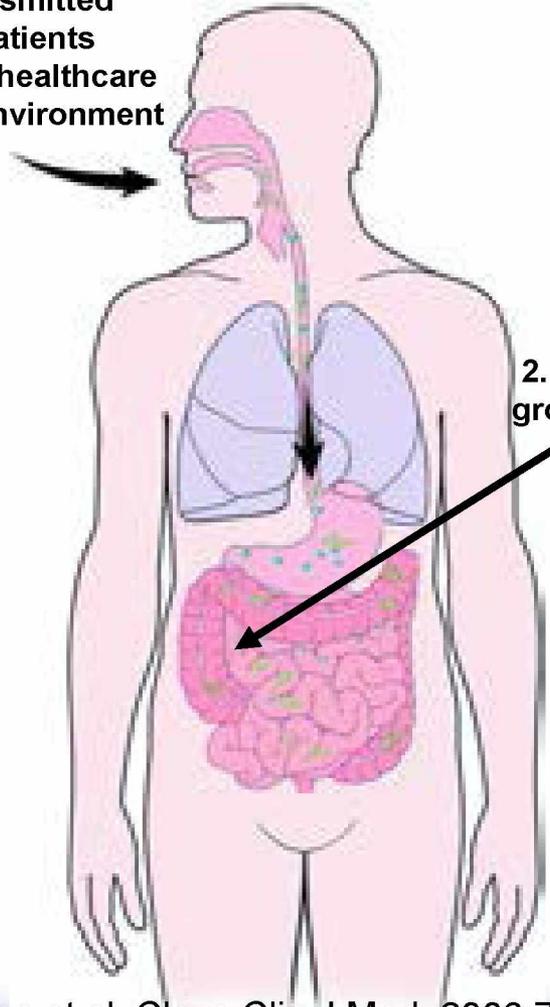
Background: HHS Prevention Targets

- **Case rate per 10,000 patient-days as measured in NHSN**
 - National 5-Year Prevention Target: 30% reduction
- **Because little baseline infection data exists, administrative data for ICD-9-CM coded *C. difficile* hospital discharges is also tracked**
 - National 5-Year Prevention Target: 30% reduction

<http://www.hhs.gov/ophs/initiatives/hai/prevtargets.html>

Background: Pathogenesis of CDI

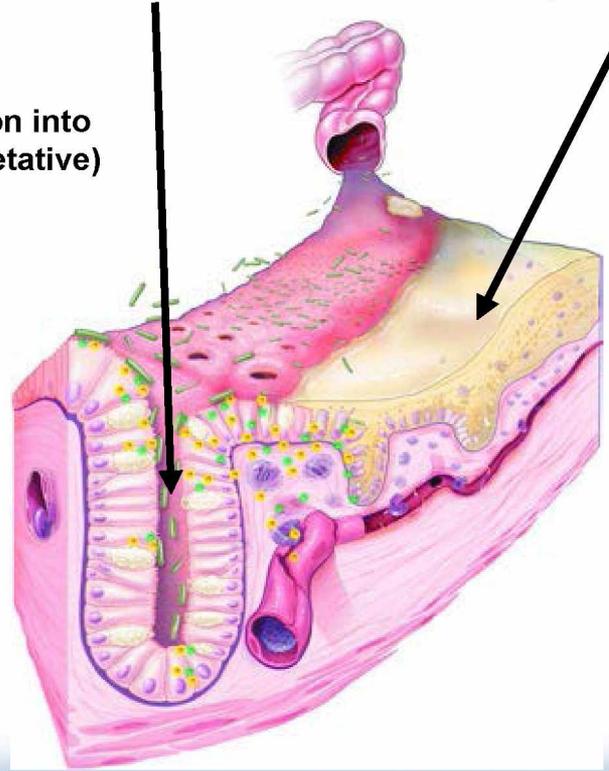
1. Ingestion
of spores transmitted
from other patients
via the hands of healthcare
personnel and environment



2. Germination into
growing (vegetative)
form

3. Altered lower intestine flora
(due to antimicrobial use) allows
proliferation of
C. difficile in colon

4. Toxin A & B Production
leads to colon damage
+/- pseudomembrane



Sunenshine et al. Cleve Clin J Med. 2006;73:187-97.



Background: Epidemiology

Current epidemic strain of *C. difficile*

- BI/NAP1/027, toxinotype III
- Historically uncommon – epidemic since 2000
- More resistant to fluoroquinolones
 - Higher MICs compared to historic strains and current non-BI/NAP1 strains
- More virulent
 - Increased toxin A and B production
 - Polymorphisms in binding domain of toxin B
 - Increased sporulation

McDonald et al. N Engl J Med. 2005;353:2433-41.

Warny et al. Lancet. 2005;366:1079-84.

Stabler et al. J Med Micro. 2008;57:771-5.

Akerlund et al. J Clin Microbiol. 2008;46:1530-3.



Background: Epidemiology Risk Factors



- Antimicrobial exposure
- Acquisition of *C. difficile*
- Advanced age
- Underlying illness
- Immunosuppression
- Tube feeds
- ? Gastric acid suppression

Main modifiable risk factors



Prevention Strategies

- **Core Strategies**
 - High levels of scientific evidence
 - Demonstrated feasibility

- **Supplemental Strategies**
 - Some scientific evidence
 - Variable levels of feasibility

The Collaborative should at a minimum include core prevention strategies. Supplemental prevention strategies also may be used. Most core and supplemental strategies are based on HICPAC guidelines. Strategies that are not included in HICPAC guidelines will be noted by an asterisk () after the strategy. HICPAC guidelines may be found at www.cdc.gov/hicpac



Prevention Strategies: Core



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- Implement an antimicrobial stewardship program
- Contact Precautions for duration of diarrhea
- Hand hygiene in compliance with CDC/WHO
- Cleaning and disinfection of equipment and environment
- Laboratory-based alert system for immediate notification of positive test results
- Educate about CDI: HCP, housekeeping, administration, patients, families

http://www.cdc.gov/ncidod/dhqp/id_CdiffFAQ_HCP.html

Dubberke et al. Infect Control Hosp Epidemiol 2008;29:S81-92.



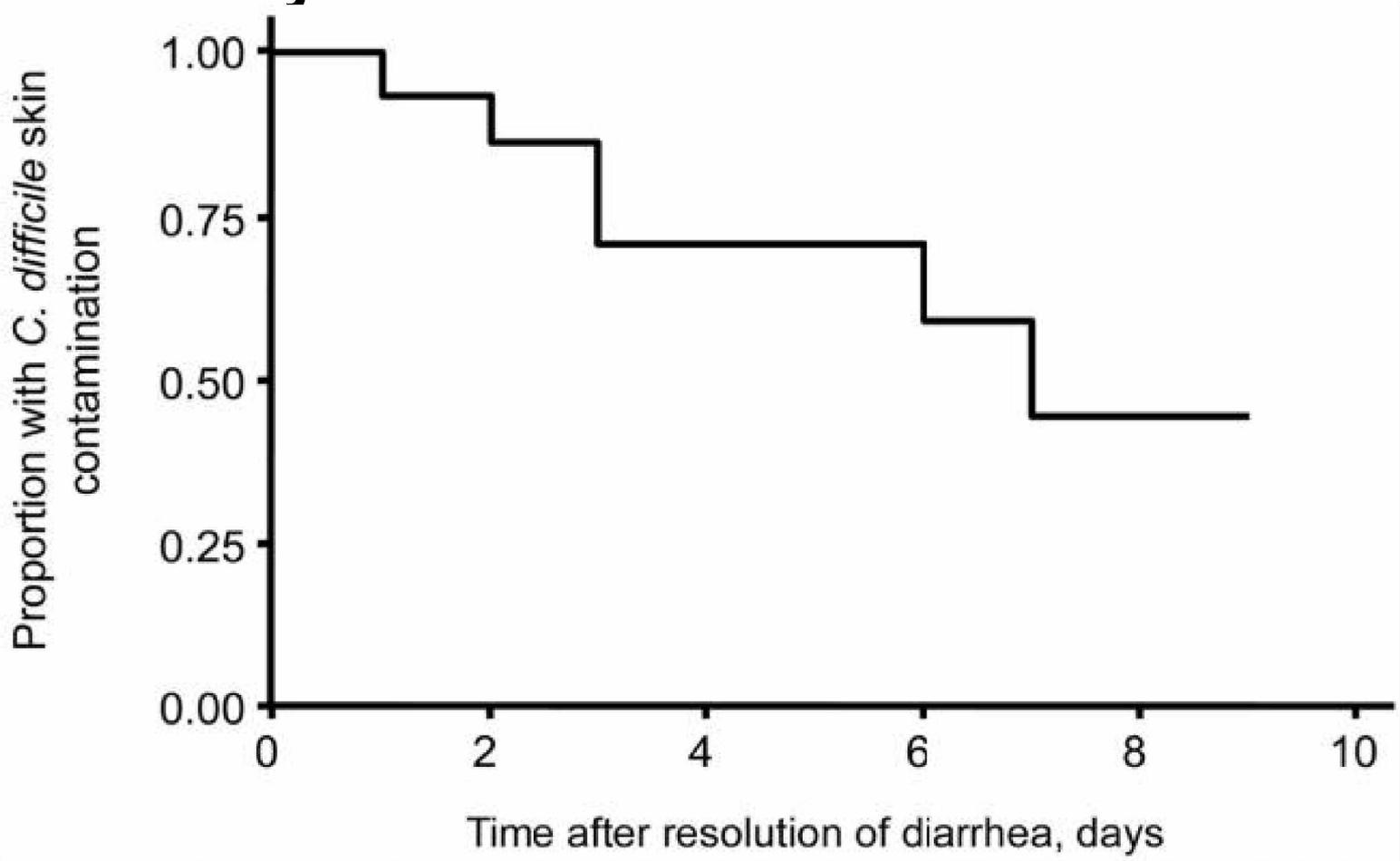
Prevention Strategies: Supplemental

- Extend use of Contact Precautions beyond duration of diarrhea (e.g., 48 hours)*
- Presumptive isolation for symptomatic patients pending confirmation of CDI
- Evaluate and optimize testing for CDI
- Implement soap and water for hand hygiene before exiting room of a patient with CDI
- Implement universal glove use on units with high CDI rates*
- Use sodium hypochlorite (bleach) – containing agents for environmental cleaning

* Not included in CDC/HICPAC 2007 Guideline for Isolation Precautions



Supplemental Prevention Strategies: Rationale for considering extending isolation beyond duration of diarrhea



Bobulsky et al. Clin Infect Dis 2008;46:447-50.



Supplemental Prevention Strategies:



Consider presumptive isolation for patients with ≥ 3 unformed stools within 24 hours

- Patients with CDI may contaminate environment and hands of healthcare personnel pending results of diagnostic testing
- CDI responsible for only ~30-40% of hospital-onset diarrhea
- However, CDI more likely among patients with ≥ 3 unformed (i.e. taking the shape of a container) stools within 24 hours
 - Send specimen for testing and presumptively isolate patient pending results
 - Positive predictive value of testing will also be optimized if focused on patients with ≥ 3 unformed stools within 24 hours
 - Exception: patient with possible recurrent CDI (isolate and test following first unformed stool)



Supplemental Prevention Strategies:

Evaluate and optimize test-ordering practices and diagnostic methods



- Most laboratories have relied on Toxin A/B enzyme immunoassays
 - Low sensitivities (70-80%) lead to low negative predictive value
- Despite high specificity, poor test ordering practices (i.e. testing formed stool or repeat testing in negative patients) may lead to many false positives
- Consider more sensitive diagnostic paradigms but apply these more judiciously across the patient population
 - Employ a highly sensitive screen with confirmatory test or a PCR-based molecular assay
 - Restrict testing to unformed stool only
 - Focus testing on patients with ≥ 3 unformed stools within 24 hours
 - Require expert consultation for repeat testing within 5 days

Peterson et al. Ann Intern Med 2009;15:176-9.



Supplemental Prevention Strategies: Hand Hygiene – Soap vs. Alcohol gel



- Alcohol not effective in eradicating *C. difficile* spores
- However, one hospital study found that from 2000-2003, despite increasing use of alcohol hand rub, there was no concomitant increase in CDI rates
- Discouraging alcohol gel use may undermine overall hand hygiene program with untoward consequences for HAIs in general

Boyce et al. Infect Control Hosp Epidemiol 2006;27:479-83.



Supplemental Prevention Strategies: Hand Washing: Product Comparison



Product	Log10 Reduction
Tap Water	0.76
4% CHG antimicrobial hand wash	0.77
Non-antimicrobial hand wash	0.78
Non-antimicrobial body wash	0.86
0.3% triclosan antimicrobial hand wash	0.99
Heavy duty hand cleaner used in manufacturing environments	1.21*

* Only value that was statistically better than others

Conclusion: Spores may be difficult to eradicate even with hand washing.

Edmonds, et al. Presented at: SHEA 2009; Abstract 43.



Supplemental Prevention Strategies: Hand Hygiene Methods



Since spores may be difficult to remove from hands even with hand washing, adherence to glove use, and Contact Precautions in general, should be emphasized for preventing *C. difficile* transmission via the hands of healthcare personnel

Johnson et al. Am J Med 1990;88:137-40.



Supplemental Prevention Strategies: Glove Use



Rationale for considering universal glove use (in addition to Contact Precautions for patients with known CDI) on units with high CDI rates

- Although the magnitude of their contribution is uncertain, asymptomatic carriers have a role in transmission
- Practical screening tests are not available
- There may be a role for universal glove use as a special approach to reducing transmission on units with longer lengths of stay and high endemic CDI rates
- Focus enhanced environmental cleaning strategies and avoid shared medical equipment on such units as well



Supplemental Prevention Strategies: Environmental Cleaning



- Bleach can kill spores, whereas other standard disinfectants cannot
- Limited data suggest cleaning with bleach (1:10 dilution prepared fresh daily) reduces *C. difficile* transmission
- Two before-after intervention studies demonstrated benefit of bleach cleaning in units with high endemic CDI rates
- Therefore, bleach may be most effective in reducing burden where CDI is highly endemic

Mayfield et al. Clin Infect Dis 2000;31:995-1000.

Wilcox et al. J Hosp Infect 2003;54:109-14.



Supplemental Prevention Strategies: Environmental Cleaning



Assess adequacy of cleaning before changing to new cleaning product such as bleach

- Ensure that environmental cleaning is adequate and high-touch surfaces are not being overlooked
- One study using a fluorescent environmental marker to assess cleaning showed:
 - only 47% of high-touch surfaces in 3 hospitals were cleaned
 - sustained improvement in cleaning of all objects, especially in previously poorly cleaned objects, following educational interventions with the environmental services staff
- The use of environmental markers is a promising method to improve cleaning in hospitals.

Carling et al. Clin Infect Dis 2006;42:385-8.



Summary of Prevention Measures

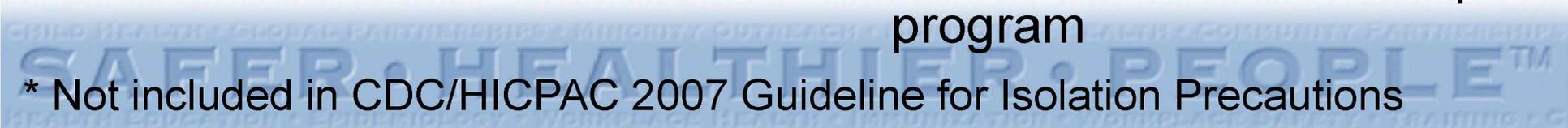
Core Measures

- Contact Precautions for duration of illness
- Hand hygiene in compliance with CDC/WHO
- Cleaning and disinfection of equipment and environment
- Laboratory-based alert system
- CDI surveillance
- Education

Supplemental Measures

- Prolonged duration of Contact Precautions*
- Presumptive isolation
- Evaluate and optimize testing
- Soap and water for HH upon exiting CDI room
- Universal glove use on units with high CDI rates*
- Bleach for environmental disinfection
- Antimicrobial stewardship program

* Not included in CDC/HICPAC 2007 Guideline for Isolation Precautions





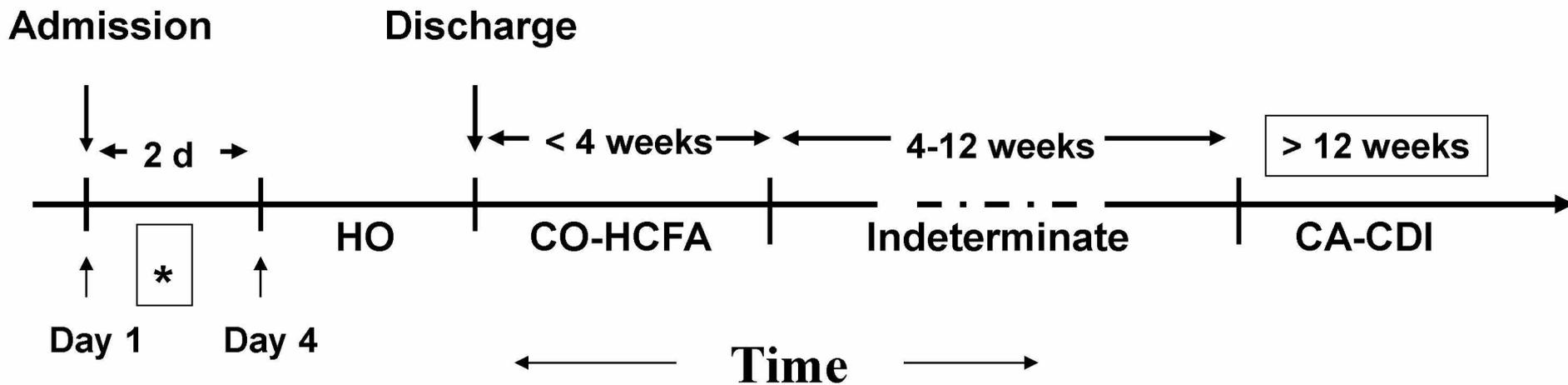
Measurement: Process Measures

- **Core Measures:**
 - Measure compliance with CDC/WHO recommendations for hand hygiene and Contact Precautions
 - Assess adherence to protocols and adequacy of environmental cleaning
- **Supplemental Measures:**
 - Intensify assessment of compliance with process measures
 - Track use of antibiotics associated with CDI in a facility



Measurement: Outcome

Categorize Cases by location and time of onset†



HO: Hospital (Healthcare)-Onset

CO-HCFA: Community-Onset, Healthcare Facility-Associated

CA: Community-Associated

* Depending upon whether patient was discharged within previous 4 weeks, CO-HCFA vs. CA

† Onset defined in NHSN LabID Event by specimen collection date

Modified from CDAD Surveillance Working Group. Infect Control Hosp Epidemiol 2007;28:140-5.



Measurement: Outcome Use NHSN CDAD Module



Laboratory-identified MDRO or CDAD Event

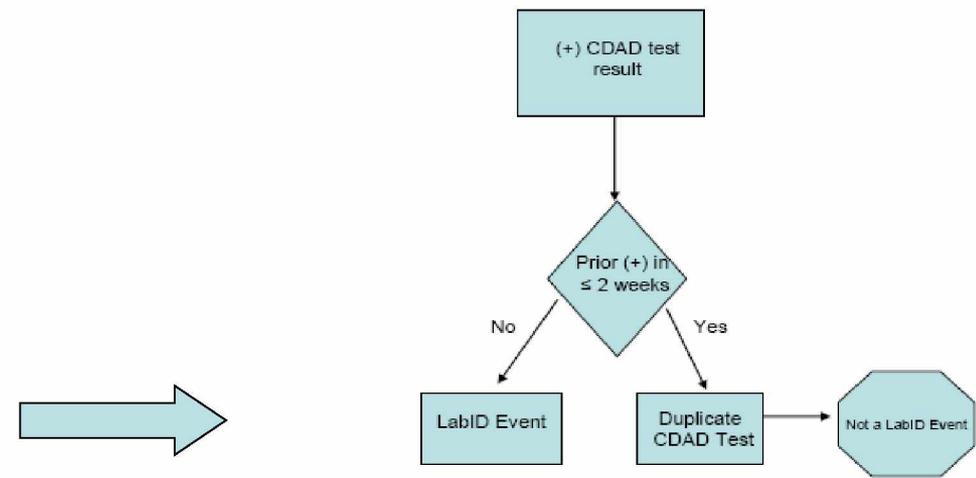
OMB No. 0920-0
Exp. Date: 03-31-12

*required for saving		
Facility ID:	Event #:	
*Patient ID:	Social Security #:	
Secondary ID:		
Patient Name, Last:	First:	Middle:
*Gender: M F	*Date of Birth:	
Ethnicity (Specify):	Race (Specify):	
Event Details		
*Event Type: LabID	*Date Specimen Collected:	
*Specific Organism Type: (Check one)		
<input type="checkbox"/> MRSA <input type="checkbox"/> MSSA <input type="checkbox"/> VRE <input type="checkbox"/> MDR- <i>Klebsiella</i> <input type="checkbox"/> MDR- <i>Acinetobacter</i> <input type="checkbox"/> C. <i>difficile</i>		
*Outpatient: Yes No	*Specimen Source:	
*Date Admitted	*Location:	*Date Admitted



Measurement: Outcome Focus on Laboratory Identified (LabID) Events in NHSN

Figure 2. CDAD Test Result Algorithm for Laboratory-Identified (LabID) Events





Measurement: Outcome

NHSN Reporting: Definitions



Based on data submitted to NHSN, CDI LabID Events are categorized as:

- **Incident:** specimen obtained >8 weeks after the most recent LabID Event
- **Recurrent:** specimen obtained >2 weeks and ≤ 8 weeks after most recent LabID Event



Measurement: Outcome

NHSN Reporting: Definitions



Incident cases further characterized based on date of admission and date of specimen collection:

- **Healthcare Facility-Onset (HO):** LabID Event collected >3 days after admission to facility (i.e., on or after day 4)
- **Community-Onset (CO):** LabID Event collected as an outpatient or an inpatient ≤ 3 days after admission to the facility (i.e., days 1, 2, or 3 of admission)
- **Community-Onset Healthcare Facility-Associated (CO-HCFA):** CO LabID Event collected from a patient who was discharged from the facility ≤ 4 weeks prior to date stool specimen collected



Measurement: Outcome



Calculating CDI Incidence Rates*

- **Healthcare Facility-Onset Incidence Rate =**
Number of all Incident HO CDI LabID Events per patient per month / Number of patient days for the facility x 10,000

- **Combined Incidence Rate =** Number of all Incident HO and CO-HCFA CDI LabID Events per patient per month / Number of patient days for the facility x 10,000

*For a given healthcare facility



Evaluation Considerations

- **Assess baseline policies and procedures**
- **Areas to consider**
 - **Surveillance**
 - **Prevention strategies**
 - **Measurement of effect of strategies**
- **Coordinator should track new policies/practices implemented during collaboration**



References

- Dubberke ER, Butler AM, Reske KA, et al. attributable outcomes of endemic *Clostridium difficile*-associated disease in nonsurgical patients. *Emerg Infect Dis* 2008;14:1031-8.
- Dubberke ER, Reske KA, Olssen MA, et al. Short- and long term attributable costs of *Clostridium difficile*-associated disease in nonsurgical inpatients. *Clin Infect Dis* 2008;46:497-504.
- Edmonds S, Kasper D, Zepka C, et al. *Clostridium difficile* and hand hygiene: spore removal effectiveness of handwash products. Presented at: SHEA 2009; Abstract 43.



References

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- Heron MP, Hoyert D, Murphy SL, et al. *Natl Vital Stat Rep* 2009;57(14). US Dept of Health and Human Services, CDC; 2009. Available at http://www.cdc.gov/nchs/data/nvsr/nvsr57/nvsr57_14.pdf



References

- Johnson S, Gerding DN, Olson MM, et al. Prospective, controlled study of vinyl glove use to interrupt *Clostridium difficile* nosocomial transmission. *Am J Med* 1990;88:137-40.
- Mayfield JL, Leet T, Miller J, et al. Environmental control to reduce transmission of *Clostridium difficile*. *Clin Infect Dis* 2000;31:995–1000.
- McDonald LC, Killgore GE, Thompson A, et al. An epidemic, toxin gene–variant strain of *Clostridium difficile*. *N Engl J Med*. 2005;353:2433-41.



References

- McDonald LC, Coignard B, Dubberke E, et al. Ad Hoc CDAD Surveillance Working Group. Recommendations for surveillance of *Clostridium difficile*-associated disease. *Infect Control Hosp Epidemiol* 2007; 28:140-5.
- Oughton MT, Loo VG, Dendukuri N, et al. Hand hygiene with soap and water is superior to alcohol rum and antiseptic wipes for removal of *Clostridium difficile*. *Infect Control Hosp Epidemiol* 2009; 30:939-44.
- Peterson LR, Robicsek A. Does my patient have *Clostridium difficile* infection? *Ann Intern Med* 2009;15:176-9
- Riggs MM, Sethi AK, Zabarsky TF, et al. Asymptomatic carriers are a potential source for transmission of epidemic and nonepidemic *Clostridium difficile* strains among long-term care facility residents. *Clin Infect Dis* 2007; 45:992–8.



References

- SHEA/IDSA Compendium of Recommendations. Infect Control Hosp Epidemiol 2008;29:S81–S92.
<http://www.journals.uchicago.edu/doi/full/10.1086/591065>
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- Sunenshine RH, McDonald LC. *Clostridium difficile*-associated disease: new challenges from and established pathogen. Cleve Clin J Med. 2006;73:187-97.



References

- Warny M, Pepin J, Fang A, Killgore G, et al. Toxin production by and emerging strain of *Clostridium difficile* associated with outbreaks of severe disease in North America and Europe. Lancet. 2005;366:1079-84.
- Wilcox MF, Fawley WN, Wigglesworth N, et al. Comparison of the effect of detergent versus hypochlorite cleaning on environmental contamination and incidence of *Clostridium difficile* infection. *J Hosp Infect* 2003;54:109-14.



Additional resources



SHEA/IDSA Compendium of Recommendations

CDI Checklist Example

581 INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY OCTOBER 2008, VOL. 29, SUPPLEMENT 1

SUPPLEMENT ARTICLE: SHEA/IDSA PRACTICE RECOMMENDATION

Strategies to Prevent *Clostridium difficile* Infections in Acute Care Hospitals

Erik R. Dubberke, MD; Dale N. Gerding, MD; David Classen, MD, MS; Kathleen M. Arias, MS, CIC;
 Kelly Podgorny, RN, MS, CPHQ; Deverick J. Anderson, MD, MPH; Helen Burstin, MD; David P. Calfee, MD, MS;
 Susan E. Coffin, MD, MPH; Victoria Fraser, MD; Frances A. Griffin, RRT, MPA; Peter Gross, MD; Keith S. Kaye, MD;
 Michael Klompas, MD; Evelyn Lo, MD; Jonas Marschall, MD; Leonard A. Mermel, DO, ScM; Lindsay Nicolle, MD;
 David A. Pegues, MD; Trish M. Perl, MD; Sanjay Saint, MD; Cassandra D. Salgado, MD, MS;
 Robert A. Weinstein, MD; Robert Wise, MD; Deborah S. Yokoe, MD, MPH

Clostridium difficile Infection (CDI) Checklist Hospital interventions to decrease the incidence and mortality of healthcare-associated *C. difficile* infections

Prevention Checklist	Treatment Checklist
<ul style="list-style-type: none"> • When an MD, PA, NP, or RN suspects a patient has CDI: <ul style="list-style-type: none"> Physician, Physician Assistant, or Nurse Practitioner: <ul style="list-style-type: none"> □ Initiate <i>Contact Precautions Plus</i> □ Order stool <i>C. difficile</i> toxin testing □ Discontinue non-essential antimicrobials □ Discontinue all anti-peristaltic medications Registered Nurse: <ul style="list-style-type: none"> □ Obtain stool sample for <i>C. difficile</i> toxin test □ Place patient in single-patient room □ Place <i>Contact Precautions Plus</i> sign on patient's door □ Ensure that gloves and gowns are easily accessible from patient's room □ Place dedicated stethoscope in patient's room □ Remind staff to wash hands with soap and water following patient contact Microbiology Laboratory Staff Person: <ul style="list-style-type: none"> □ Call relevant patient floor with positive <i>C. difficile</i> toxin test result □ Provide daily list of positive test results for Infection Control Infection Control Practitioner: <ul style="list-style-type: none"> □ Check microbiology results daily for positive <i>C. difficile</i> toxin results □ Call relevant floor to confirm that patient with positive <i>C. difficile</i> toxin results is in a single-patient room and that the <i>Contact Precautions Plus</i> sign is on the patient's door □ Flag the patient's <i>C. difficile</i> status in the hospital's clinical information system or in the patient's paper chart □ Alert housekeeping that the patient is on <i>Contact Precautions Plus</i> Environmental Services Staff Person: <ul style="list-style-type: none"> □ Prior to discharge cleaning, check for <i>Contact Precautions Plus</i> sign on the patient's door □ If <i>Contact Precautions Plus</i> sign is on the door, clean the room with a bleach-based cleaning agent □ Confirm for supervisor that bleach-based cleaning agent was used for discharge cleaning for every patient on <i>Contact Precautions Plus</i> 	<ul style="list-style-type: none"> • When an MD, PA, or NP diagnoses mild CDI: <i>All of the following criteria are present: diarrhea (>3 BM/day), no fever, WBC <15,000, no peritoneal signs, and no evidence of sepsis.</i> <ul style="list-style-type: none"> Physician, Physician Assistant, or Nurse Practitioner: <ul style="list-style-type: none"> □ Initiate oral metronidazole at dose 500mg every 8 hours □ If no clinical improvement by 48-72 hours after diagnosis, treat patient as moderate CDI □ Continue therapy for at least 14 days total and at least 10 days after symptoms have abated • When an MD, PA, or NP diagnoses moderate CDI: <i>At least one of the following criteria is present: diarrhea (<12 BM/day), fever 37.5-38.5°C, WBC 15,000-25,000, or frankly visible stable lower gastrointestinal bleeding.</i> <ul style="list-style-type: none"> Physician, Physician Assistant, or Nurse Practitioner: <ul style="list-style-type: none"> □ Initiate oral vancomycin at dose 250mg every 6 hours □ If no clinical improvement by 48 hours, add IV metronidazole at dose 500mg every 8 hours □ Consider obtaining infectious disease consultation □ Consider obtaining abdominal CT scan □ Continue therapy for at least 14 days total and at least 10 days after symptoms have abated • When an MD, PA, or NP diagnoses severe CDI: <i>At least one of the following criteria is present: diarrhea (>12 BM/day), fever >38.5°C, WBC >25,000, hemodynamic instability, marked & continuous abdominal pain, ileus, absence of bowel sounds, evidence of sepsis, or intensive care unit level of care required.</i> <ul style="list-style-type: none"> Physician, Physician Assistant, or Nurse Practitioner: <ul style="list-style-type: none"> □ Obtain immediate infectious disease consultation □ Obtain immediate general surgery consultation □ Obtain abdominal CT scan □ Initiate oral vancomycin at dose 250mg every 6 hours together with IV metronidazole at dose 500mg every 6 hours □ Following consultation with general surgery regarding its use, consider rectal vancomycin □ Ask general surgery service to assess the need for colectomy

Abbreviations: MD=medical doctor, PA=physician assistant, NP=nurse practitioner, RN=registered nurse, BM=bowel movement, WBC=white blood cell count, CT=computed tomography, IV=intravenous

FIGURE 1. *Clostridium difficile* infection checklist at Brigham and Women's Hospital.

Dubberke et al. Infect Control Hosp Epidemiol 2008;29:S81-92.
 Abbett SK et al. Infect Control Hosp Epidemiol 2009;30:1062-9.





Additional Reference Slides



- The following slides may be used for presentations regarding CDI.
- Explanations are available in the notes section of the slides.



Supplemental Prevention Strategies:



Rationale for Soap and Water: Lack of efficacy of alcohol-based handrub against *C. difficile*

Interventions compared		Mean log reduction (95% CI), log ₁₀ CFU/mL
Intervention 1	Intervention 2	
Warm water and plain soap	No hand hygiene	2.14 (1.74–2.54)
Warm water and plain soap	Alcohol-based handrub	2.08 (1.69–2.47)
Cold water and plain soap	No hand hygiene	1.88 (1.48–2.28)
Cold water and plain soap	Alcohol-based handrub	1.82 (1.43–2.22)
Warm water and plain soap	Antiseptic hand wipe	1.57 (1.18–1.96)
Warm water and antibacterial soap	No hand hygiene	1.51 (1.12–1.91)
Warm water and antibacterial soap	Alcohol-based handrub	1.46 (1.06–1.85)
Cold water and plain soap	Antiseptic hand wipe	1.31 (0.92–1.71)
Warm water and antibacterial soap	Antiseptic hand wipe	0.94 (0.55–1.34)
Warm water and plain soap	Warm water and antibacterial soap	0.63 (0.23–1.02)
Antiseptic hand wipe	No hand hygiene	0.57 (0.17–0.96)
Antiseptic hand wipe	Alcohol-based handrub	0.51 (0.12–0.91)
Cold water and plain soap	Warm water and antibacterial soap	0.37 (–0.03 to 0.76)
Warm water and plain soap	Cold water and plain soap	0.26 (–0.14 to 0.66)
Alcohol-based handrub	No hand hygiene	0.06 (–0.34 to 0.45)

Oughton et al. Infect Control Hosp Epidemiol 2009;30:939-44.



Supplemental Prevention Strategies: Hand Hygiene – Alcohol Hand Rub Use 2000-2003

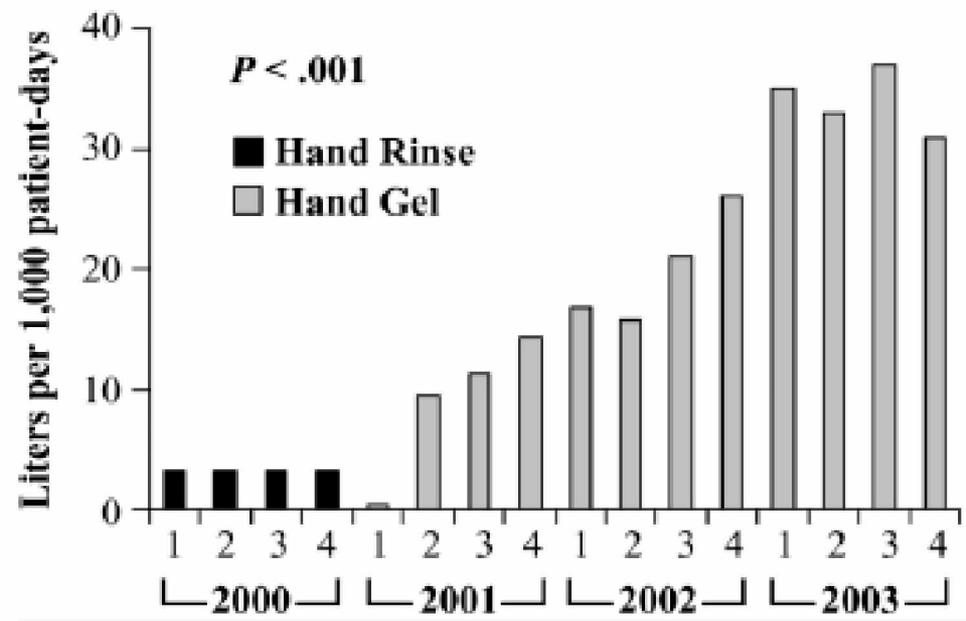


FIGURE 1. Use of alcohol hand rub by healthcare workers, in liters per 1,000 patient-days, per quarter, 2000-2003.

Boyce et al. Infect Control Hosp Epidemiol 2006; 27:479-83.



Supplemental Prevention Strategies: Hand Hygiene – CDI Rates 2000-2003

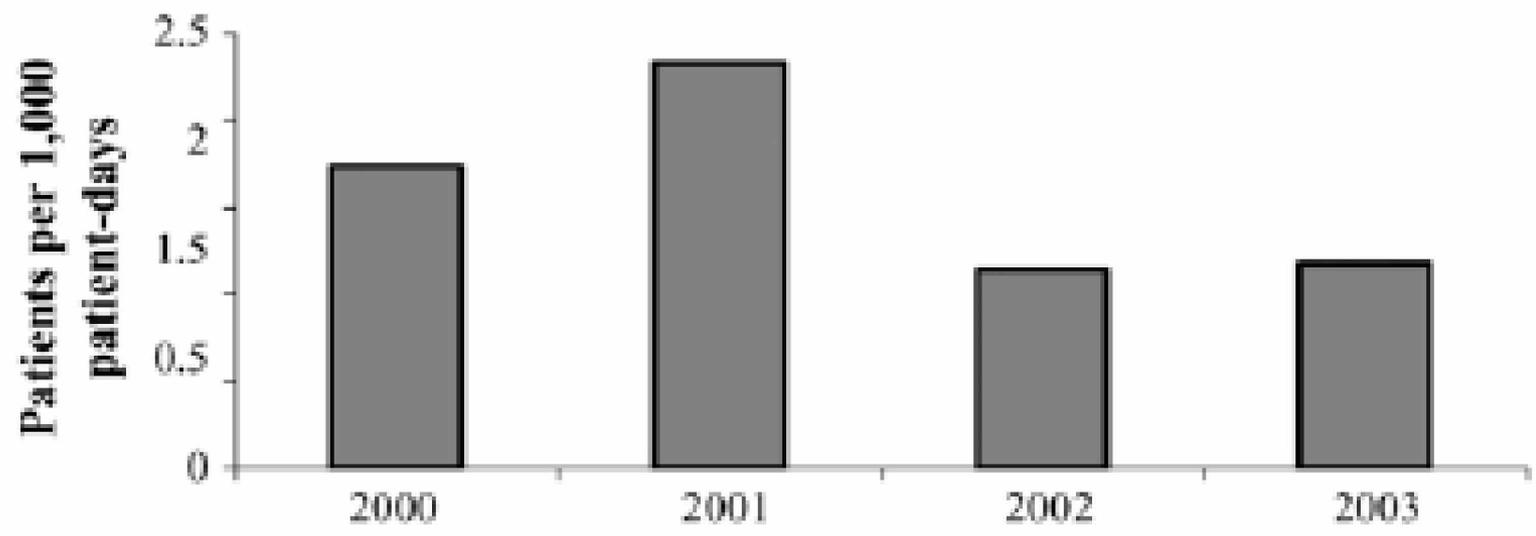


FIGURE 2. Number of patients with 1 or more tests positive for *Clostridium difficile* toxin per 1,000 patient-days, 2000-2003.

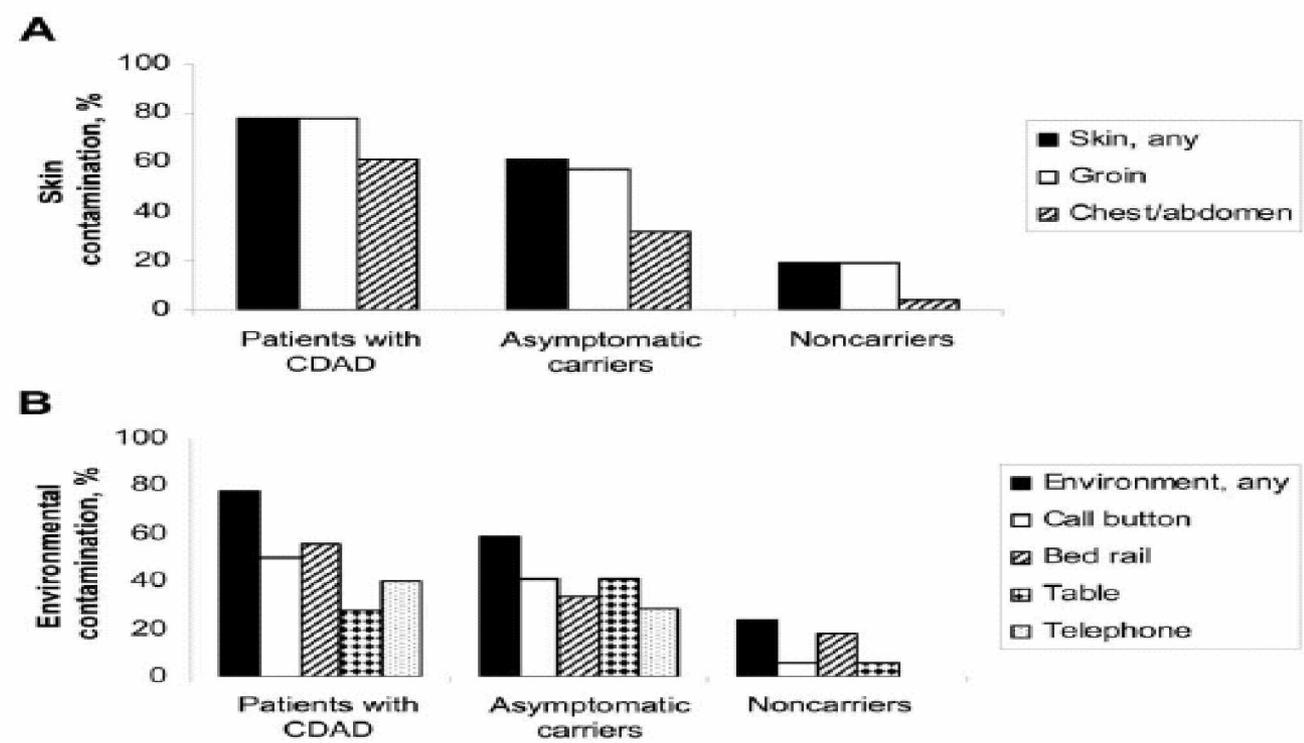
Boyce JM et al. Infect Control Hosp Epidemiol 2006; 27:479-83.



Supplemental Prevention Strategies: Universal Glove Use

Role of asymptomatic carriers?

Rationale for universal glove use on units with high CDI rates



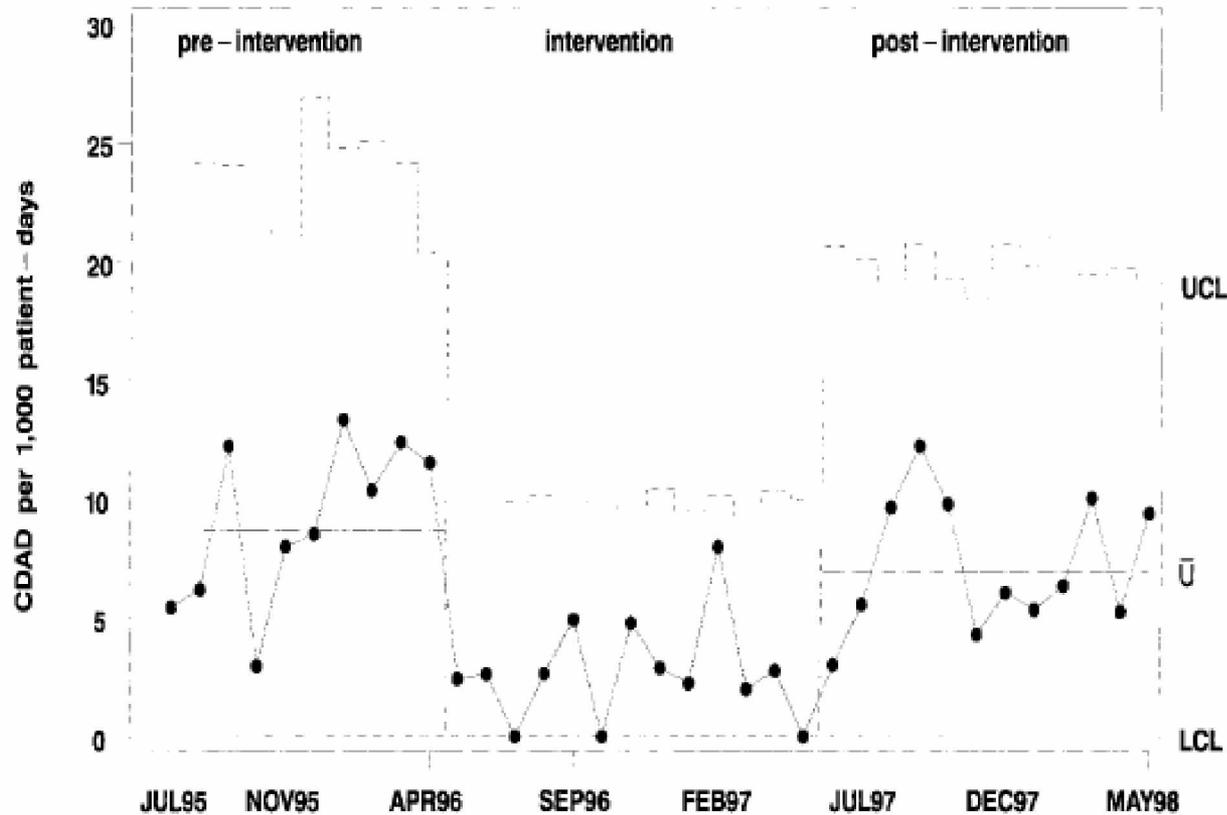
Riggs et al. Clin Infect Dis 2007;45:992-8.



Supplemental Prevention Strategies: Environmental Cleaning



How Much Can be Achieved via Environmental Decontamination?



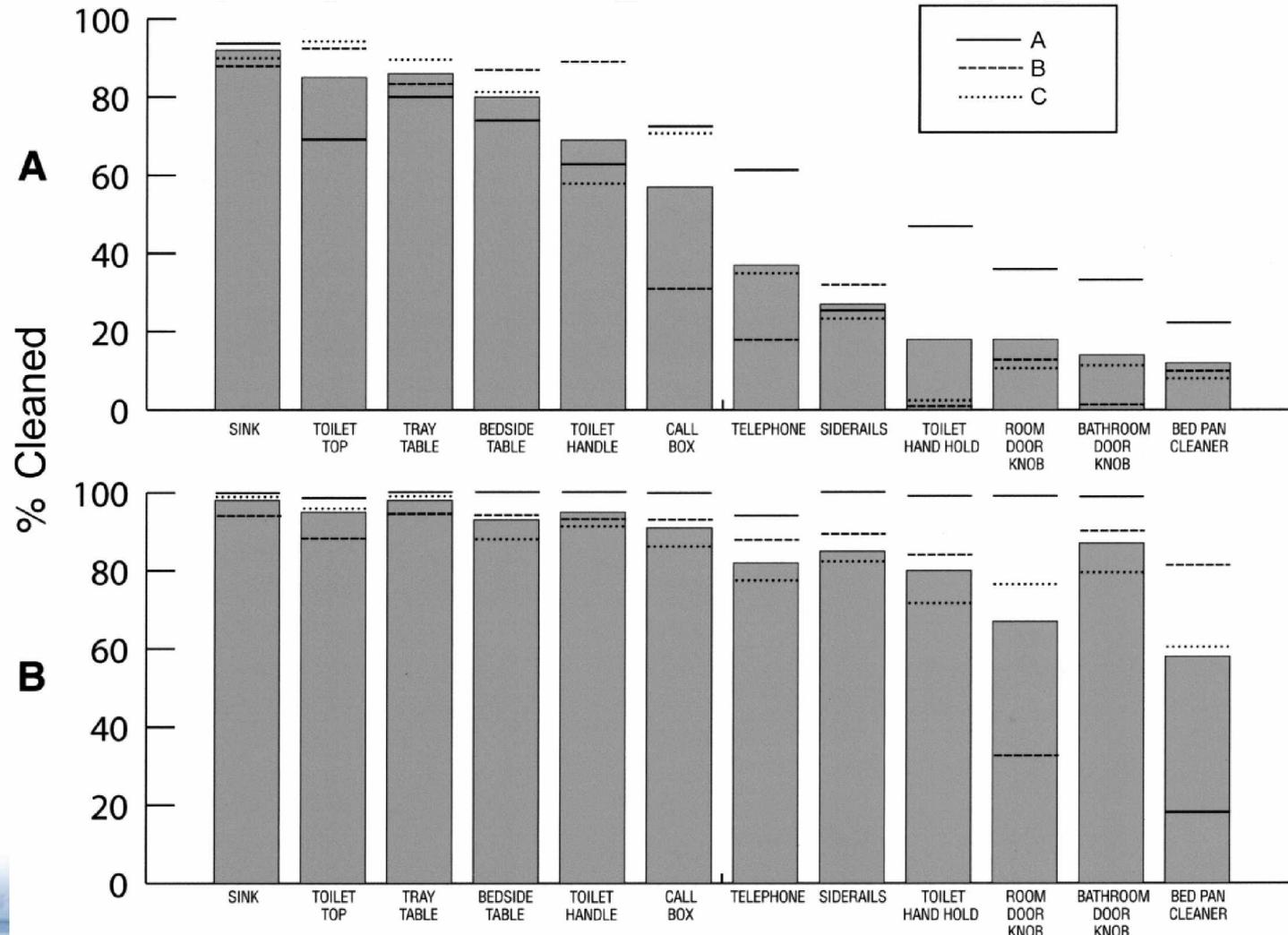
Mayfield et al. Clin Infect Dis 2000;31:995–1000.



Supplemental Prevention Strategies: Environmental Cleaning

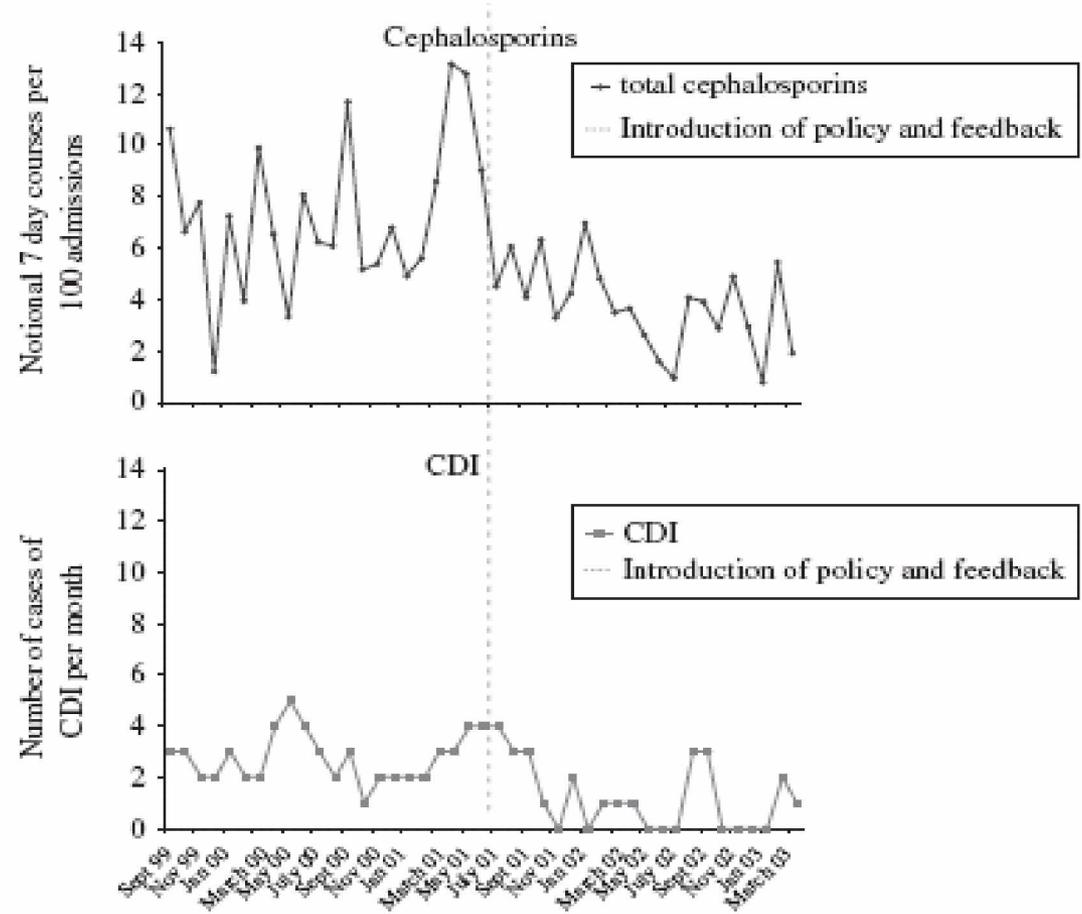


Assess adequacy of cleaning before changing to new cleaning





Supplemental Prevention Strategies: Audit and feedback targeting broad-spectrum antibiotics



Fowler et al. J Antimicrob Chemother 2007;59:990-5.